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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/573,352

03/24/2006

Robert Hugh Bradbury

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03/05/2009

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EXAMINER

TRUONG, TAMTHOM NGO

ART UNIT

PAPER NUMBER

1624

MAIL DATE

DELIVERY MODE

03/05/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/573,352	Applicant(s) BRADBURY ET AL.	
	Examiner TAMTHOM N. TRUONG	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11-4-08 (Election).
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-32 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-32 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11/4/08, 1/9/07, 3/24/06</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

In the response of 11-4-08, applicants have elected with traverse the species of group b (A is a phenyl group). The traversal is on the ground that there is no serious burden of searching. However, the claims must be searched and examined according to different rings represented by A. Thus, the election of species is deemed proper, and therefore, made FINAL.

Claims 1-32 are pending.

\35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Use Claim: Claim 30 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

- a. Claim 1 and dependent claims recite many limitations in parentheses which are not clear if they are part of the claims (e.g., "(provided the ring is not thereby quaternised)", "(on any available carbon atoms)").
- b. Claim 1 has unmatched parentheses (e.g., page 169, line 17).
- c. **Use Claim:** Claim 30 provides for the use of formula I, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.
- d. Claims 28-31 lack antecedent basis because they depend on claim 1, but recite "prodrug form thereof" which is not recited in claim 1. The specification does not define what constitutes a "prodrug form".

e. Claim 31 recites the limitation of “anti-proliferative effect” which is not clear what diseases or organs are intended. The specification does not define what constitutes “anti-proliferative effect”.

f. Claim 32 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language. Claim 32 recites the limitation of “removed by conventional means”. This claim is an omnibus type claim.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Scope of Enablement (for prodrug): Claims 28-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making salts of the claimed compounds, does not reasonably provide enablement for making “*prodrug*” of the claimed compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

- (1) The breadth of the claims;
- (2) The amount of direction or guidance presented;
- (3) The state of the prior art;
- (4) The relative skill of those in the art;
- (5) The predictability or unpredictability of the art;
- (6) The quantity of experimentation necessary;

[See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

The breadth of the claims: Claims 28-31 recite “prodrug” of compounds represented by formula I. The term “prodrug” covers just about any ester, amide, phosphate, sulfate having an infinite combination of functional groups, rings, substituents, etc., and could drastically alter the structure of the parent compound. **The amount of direction or guidance presented:** Although the specification briefly defines what “prodrug” is, it does not provide working examples to guide the skilled chemist to select a particular ester, amide, phosphate or sulfate for a particular site on the parent compound in order to obtain a “prodrug”.

The state of the prior art: Although it is not unusual to expect a “prodrug” of a compound, the process for selecting a particular ester, amide, phosphate, sulfate, hydrate or solvate is not standard for all drugs. For the claimed compound, there is no reference teaching any possible prodrug. Thus, the state of the prior art does not support the broad scopes of claims 28-31.

The relative skill of those in the art: Even with the advanced training, the skilled clinician would have to engage in extensive research to select a particular “prodrug” for each compound from the large Markush group of formula I. Not only one has to determine an IC_{50} value, but also *in-vivo* activity to establish an LD_{50} , therapeutic index and active metabolites for each “prodrug”. Given a large Markush group of formula I, such a task would require a tremendous amount of effort, time and resource.

The predictability or unpredictability of the art & The quantity of experimentation necessary: The process of making a prodrug requires three criteria: (1) the “prodrug” must be biologically inactive; (2) the “prodrug” must be metabolized into the active drug at a physiologically meaningful concentration; (3) the active drug must still have the intended biological activity. Many prodrugs produce additional active metabolites (*in- vivo*) that do not have the same chemical structure of the intended drug. Thus, the process of making a prodrug is highly unpredictable due to many unknown *in-vivo* factors as well as uncertain numbers of active metabolites with potential adverse effects.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TAMTHOM N. TRUONG whose telephone number is (571)272-0676. The examiner can normally be reached on M, T and Th (9:00-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Tamthom N. Truong/
Examiner, Art Unit 1624

/James O. Wilson/
Supervisory Patent Examiner, Art Unit 1624

Tamthom N. Truong
Patent Examiner, Art Unit 1624

2-27-09